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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/478,621 | 01/05/2000 | Stephen E. Epstein | 674522-2001 | 1917 |

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EXAMINER

JIANG, DONG

ART UNIT PAPER NUMBER

1646

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/478,621 | EPSTEIN ET AL. | |
| | Examiner | Art Unit | |
| | Dong Jiang | 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 August 2004.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 22 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

DETAILED OFFICE ACTION

Applicant's amendment and response filed on 17 August 2004 is acknowledged and entered. Following the amendment, claims 18-21 and 23-25 are canceled, and claim 22 is amended.

Currently claim 22 is pending, and under consideration.

Note: according to the "Revised Format of Amendment", the status of the present claim 22 should be designated as "currently amended" since the claim has been amended.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite because the claim does not specify the amount of the protein agents being used in the method for "reducing risk of restenosis" (preamble), nor the endpoint, for example, "in an amount effective to ...". The metes and bounds of the claim, therefore, cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention, for the reasons of record set forth in the last Office Action mailed on 17 May 2004, at pages 3-4.

Applicants argument filed on 17 August 2004 has been fully considered, but is not deemed persuasive for reasons below.

At pages 3-4 of the response, the applicant argues that MPEP states that “lack of working examples or lack of evidence that the claimed invention works as described should not never be the sole reason for rejecting the claimed invention on the ground of lack of enablement”; that claim 22 has been amended to reflect the disclosure of Example 2; that one of skill in the art would face no undue experimentation in administering a soluble VEGF receptor and angiopoietin-1 following balloon angioplasty; and that applying *Wands* factors to the instant facts, enablement is shown to exist, and the amount of experimentation necessary is low, while the amount of direction is high. This argument is not persuasive because the instant rejection was not only based on the sole reason of lack of working examples or evidence, rather, other *Wands* factors were also in consideration, such as the state of the prior art, the large quantity of experimentation necessary, the nature of the invention, and the lack of predictability. For example, as addressed in the last Office Action, the prior art by Pels teaches that adventitial microvessels have a beneficial impact on the maintenance of arterial lumen after the injury, which is just the opposite of what is taught in the present application, and *teaches away* from the claimed invention. Therefore, in the absence of working examples or any direct evidence in the instant application to support the contrary claims, it is not predictable whether the present method would be beneficial for treating restenosis, and undue experimentation would be required in order to determine such prior to the clinical application as claimed. Further, with respect to the nature of the invention, which is directed to a method of treatment by administering protein agents, the working example relied upon teaches the gene therapy, which is very different from protein therapy as it requires the production of the encoded protein *in vivo* first in order to achieve any desired effect, and the proper expression of the protein from a transgene is often not predictable. In the present Example 2, it is unclear whether the transgenes of the adenoviral vector administered were ever expressed. Therefore, it is impossible for one of skilled in the art to determine based on the teachings of Example 2 whether the gene therapy worked at all, how well it worked if it were effective, and whether the *claimed* method of *protein* therapy would

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work at all. In *In re Fisher*, 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970), the court clearly states:

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

In the present case, the specification discloses an example of gene therapy without demonstrating the expression of the protein encoded by the transgene. Therefore, it is unpredictable whether the claimed protein therapy would be effective based on such an example, and the claims are not sufficiently supported under the first paragraph of 35 U.S.C. 112. Thus, further experimentation would be required to answer above questions, and it is, by no means, a *routine* experimentation.

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
10/20/04